Synthesis and Complexation of an Optically Active Aza-Crown Ether (Commemoration Issue Dedicated to Professor Yuzo Inouye on the Occasion of his Retirement)

AUTHOR(S):

Kawakami, Yukio; Yamamoto, Yukio; Oda, Jun'ichi; Inouye, Yuzo; Sawada, Seiji

CITATION:

Kawakami, Yukio ...[et al]. Synthesis and Complexation of an Optically Active Aza-Crown Ether (Commemoration Issue Dedicated to Professor Yuzo Inouye on the Occasion of his Retirement). Bulletin of the Institute for Chemical Research, Kyoto University 1983, 61(2): 117-119

ISSUE DATE:

1983-08-15

URL:

http://hdl.handle.net/2433/77025

Bull. Inst. Chem. Res., Kyoto Univ., Vol. 61, No. 2, 1983

COMMUNICATION

Synthesis and Complexation of an Optically Active Aza-Crown Ether

Yukio KAWAKAMI*, Yukio YAMAMOTO*, Jun'ichi ODA*,
Yuzo INOUYE*, and Seiji SAWADA**

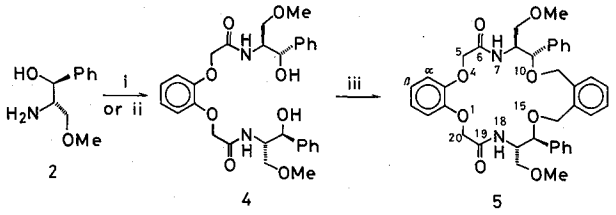
Received April 14, 1983

A variety of macrocyclic polyethers have been synthesized and investigated since the discovery of the excellent chemical performances of crown ethers.[1] Among them, chiral macrocyclic polyethers[2] which have been the target of artificial enzymes are also of interest from the viewpoint of ionophore models; cyclic polypeptides like crown ethers exhibit the selectivity toward specific metal cations and associate with such biological activities as antibiotics. We wish to report here the synthesis and the cation-binding ability of an optically active aza-crown ether **5** from (1*S*, 2*S*)-(+)-2-amino-1-phenyl-1,3-propandiol (**1**).

The O-methyl amino-alcohol **2** was prepared from **1** *via* oxazoline derivatives according to Meyers.[3] The DCC condensation of **2** and *o*-phenylenedioxydiacetic acid (**3**) derived from pyrocatechol and chloroacetic acid[4] gave the dihydroxy-diamide **4** in 34% yield; mp 111–112°C, $[\alpha]_D^{20}$ +63.7° (c=1.01, $CHCl_3$), IR ν_{max}^{KBr} cm^{-1}: 3400(OH), 1670 (N–C=O), 740 and 705 (phenyl), ^1H NMR($CDCl_3$) δ: 3.27, (6H, singlet), 4.50 (4H, singlet), 4.90 (2H, doublet), 6.64–7.00 (4H, multiplet), 7.27 (10H, singlet). Alternatively, **4** was also prepared through the *p*-nitrophenyl ester of **3** in 47% yield. By the action of sodium hydride and α, α'-dibromo-*o*-xylene in DMSO, **4** was converted to the macrocyclic amide polyether, (8*S*, 9*S*, 16*S*, 17*S*)-8, 17-bis (methoxymethyl)-9, 16-diphenyl-2, 3, 12, 13-dibenzo-6, 19-dioxa-7, 18-diaza-1, 4, 10, 15-tetraoxy-2, 12-cycloeicosadiene, (**5**) in 40% yield; glass, $[\alpha]_D^{20}$ +103.3° (c=1.2, $CHCl_3$), MS m/z: 654 (M^+), IR ν_{max}^{KBr} cm^{-1}: 2940 (CH), 1690 (N–C=O), ^1H NMR (CD_3CN) δ: 3.16–3.29 (2H, multiplet), 3.19 (6H, singlet, OCH_3), 4.12–4.61 (6H, multiplet), 4.43 (4H, singlet, H-11 and 14), 4.49 (4H, singlet, H-5 and 20), 7.00 (4H, singlet, H-α and β), 7.00–7.20 (2H, broad singlet, H-7 and 18), 7.23 (4H, singlet, phenylene with C-12 and 13), 7.36 (10H, singlet, phenyl at C-9 and 16), ^{13}C NMR (CD_3CN) δ: 55.05 (C-8 and 17), 59.02 (OCH_3), 69.79 (C-11 and 14), 70.32 (methylene at C-8 and 17), 72.48 (C-9 and 16), 81.43 (C-5 and 20), 116.01, 123.73, 148.89 (phenylene with C-2 and 3), 128.41, 128.65, 129.46, 140.35 (phenyl at C-9 and 16), 129.15, 129.88, 137.36 (phenylene with C-12 and 13), 168.84 (C-6 and 19).

* 川上幸夫，山本行男，小田順一，井上雄三: Laboratory of Plant Product Chemistry, Institute for Chemical Research, Kyoto University, Uji, Kyoto 611.

** 沢田誠二: Department of Chemistry, Kyoto Universisty of Education, Fushimi, Kyoto 612.



Scheme 1. i, *o*-phenylenedioxydiacetic acid, DCC; ii, di-*p*-nitrophenyl *o*-phenylenedioxydiacetate; iii, NaH, α, α'-dibromo-*o*-xylene.

The cation-binding ability of the amide crown ether **5** with lithium, sodium, and magnesium perchlorates was assessed by CD and NMR spectroscopies in acetonitrile. In CD spectra, the ellipticity for the native **5** was 4.6×10^4 degree·cm^2/dmol (217 nm) and complexation with magnesium and lithium ions increased the molar ellipticity up to 20%. The association constants, log *Ka*, were estimated to be 2.5 and 1.9 to magnesium and lithium ions, respectively, according to the literature[5] which assumed a complex composed of one metal ion and one ligand.[6] On the other hand, sodium ion formed no complex with **5**.[7] The induced shift by adding equimolar amounts of the metal perchlorates in ^{13}C NMR and ^{1}H NMR spectra also supported the above trend. Not only carbonyl oxygens (C-6 and 19) but also oxygens (O-1 and 4) of phenolic function participated with the complexation because the peaks of carbonyl oxygens (C-6 and 19), aromatic carbons and protons (C-α and C-β), and methylene protons (at C-5 and 20) adjacent to carbonyl groups shifted toward downfield.[9] The oxygen atoms sticking out of the ring turned out to be irrelevant to the complexation.

Acknowledgment. This study was supported in part by a Grant-in-Aid for Developmental Scientific Research (No. 57760100, in 1982–1983) from the Ministry of Education, Science and Culture of Japan, for which the authors' thanks are due.

REFERENCES AND NOTES

(1) C. J. Pedersen, *J. Am. Chem. Soc.*, **89**, 7017 (1967).
(2) Y. Chao and D. J. Cram, *ibid.*, **98**, 1015 (1976); F. Wudl and F. Gaeta, *J. Chem. Soc., Chem. Commun.*, **1972**, 107; R. C. Helgeson, K. Koga, J. M. Timko, and D. J. Cram, *J. Am. Chem. Soc.*, **95**, 3021 (1973); R. C. Helgeson, J. M. Timko, and D. J. Cram, *ibid.*, **95**, 3023 (1973); T. Matsui and K. Koga, *Tetrahedron Lett.*, **1978**, 1115.
(3) A. I. Meyers, G. Knaus, K. Kamata, and M. E. Ford, *J. Am. Chem. Soc.*, **98**, 567 (1976).
(4) C. A. Bischoff and E. Fröhlich, *Chem. Ber.*, **40**, 2779 (1907).
(5) M. P. Mack, R. R. Hendrixson, R. A. Palmer, and R. G. Ghirardelli, *J. Am. Chem. Soc.*, **98**, 7830 (1976); J. Grandjean, P. Laszlo, J. P. Picavet, and H. Sliwa, *Tetrahedron Lett.*, **1978**, 1861.
(6) The concentration of **5** was 1.63×10^{-6}mol/l and the salts were added up to 5000-fold amounts.
(7) The association constant, log *Ka*, of **5** and *t*-butylammonium thiocyanate in $CDCl_3$ measured according to Cram's procedure[8] was shown to be less than 2.4.
(8) J. M. Timko, S. S. Moore, D. M. Walba, P. C. Hiberty, and D. J. Cram, *J. Am. Chem. Soc.*, **99**, 4207 (1977).

(9) With magnesium ion, downfield shifts of 1.87 ppm (C-6 and 19), 0.53 ppm, and 0.47 ppm (C-α and β) in ^{13}C NMR and 0.083 ppm (protons at C-5 and 20) and 0.067 ppm (protons at C-α and β) in ^{1}H NMR. With lithium ion, downfield shifts of 1.05 ppm (C-6 and 19) and 0.24 ppm (C-α and β) in ^{13}C NMR and 0.017 ppm (C-5 and 20) and 0.033 ppm (protons at C-α and β) in ^{1}H NMR.